REMARKS

Claims 1, 2, 4-10, 13-19 are pending and have been rejected. Claims 3, 11-12, and 20-60 have been canceled.

Double Patenting

Claims 1, 2, 4-10, and 13-19 have been rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,765,001.

Without conceding to the Examiner's characterizations, Applicant herewith submits a terminal disclaimer in compliance with 37 C.F.R. §1.321(c). (Attached as Exhibit 1 hereto). As such, the rejection is moot and Applicant requests the rejection be withdrawn.

35 U.S.C. § 103(a)

A. Claims 1, 2, 4-10, and 13-19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Poulsen (US 3,934,013).

Applicant respectfully traverses this rejection. The Examiner fails to establish a *prima facie* case of obviousness based on Poulsen with regard to the present invention.

35 U.S.C. §103(a) sets forth in part:

> [a] patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject mater as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said matter pertains.

PAGE 7/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

To establish a *prima facie* case of obviousness the prior art reference (or references when combined) must teach or suggest all of the claim limitations. MPEP §2142; *Velander v. Garner*, 348 F.3d 1359, 1363 (Fed. Cir. 2003).

According to the Supreme Court, obviousness should be determined by examining (1) the scope and content of the prior art, (2) the differences between the claimed invention and the prior art, and (3) the level of ordinary skill in the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (February 21, 1966); see also *KSR International, Co. v. Teleflex Inc., et al.*, 127 S. Ct. 1727 (2007). The Supreme Court also identified certain objective evidence of nonobviousness, such as commercial success, long felt but unresolved needs, and failure of others. *Id.*

Applicant agrees with the Examiner that Poulsen "does not teach some of the particular percentages of corticosteroid or propylene glycol herein." *See* Office Action mailed May 16, 2007, p. 3. In addition to not teaching or suggesting the particular percentages of corticosteroid or propylene glycol, Poulsen also does not teach or suggest the claimed PE Ratio (defined below) or the use of two or more penetration enhancers. The Examiner asserts that "the fatty alcohol or ester is considered as [sic] to meet the limitation of penetration enhancer since it is well known that fatty compound would enhance the penetration of topical therapeutical compounds. See, e.g., page 2, third paragraph in the specification." *See* Office Action mailed May 16, 2007, p. 3. However, the Examiner's assertion is misplaced and misinterprets the meaning of page 2, third paragraph of the present specification.

Poulsen states that "[s]uitable fatty alcohols include cetyl alcohol, stearyl alcohol, behenyl alcohol and the like." Col. 10, lines 47-49. The fatty alcohols described in Poulsen are not penetration enhancers. Rather, the fatty alcohols disclosed are known to be emulsifiers and

PAGE 8/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

emollients. Further, as described in the instant specification at paragraph 34, stearyl alcohol is defined as a non-solvent/emulsifier not a penetration enhancer. Additionally, cetyl alcohol and behenyl alcohol are not described in the instant specification as being penetration enhancers.

Poulsen also does not teach or suggest a ratio of penetration enhancers to penetration enhancers and solvents and emulsifiers ("PE Ratio") of at least about 0.90. Pouslen also does not teach or suggest two or more penetration enhancers and some of the specific amounts of corticosteroids and propylene glycol. In addition to not teaching two or more penetration enhancers and a PE Ratio of at least about 0.90 and above; Poulsen also does not teach or suggest (or even recognize) the novel and critical factors that are used in the PE Ratio calculation or that the PE Ratio results in particular vasoconstrictor scores.

Since Poulsen is silent about the two or more penetration enhancers, the PE Ratio, and a PE Ratio of at least about 0.90, one of ordinary skill in the art would not have been motivated to employ the corticosteroid(s) and penetration enhancers of the present invention, much less in the amounts necessary to achieve a PE Ratio of at least about 0.90. Further, for optimization of a particular Result-Effective Variable (such as the PE Ratio) to be considered obvious, the particular variable must first be recognized, which is not the case with the prior art of record. MPEP §2144.05. Poulsen's silence regarding particular elements of the claimed invention cannot and does not lend itself to mere optimization and thus, the claimed invention is not obvious over the prior art.

It is important to point out that the PE Ratio is a Result-Effective Variable which is a critical and novel aspect of the present invention. There is no teaching or suggestion in the prior art to use the specified components in the claimed PE Ratio or that such a PE Ratio correlates

PAGE 9/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

between improved potency and unexpectedly high vasoconstrictor scores. A declaration by Dr. Gans, a named inventor of the present invention, was filed in the parent case (U.S. 6,765,001) (a copy of which is attached hereto) showing that vasoconstrictor scores serve as a measure of the inherent potency of a drug and that a PE Ratio of 0.90 and above surprisingly resulted in an average vasoconstrictor score of 85, which is above the minimum score of 80 required by the FDA for Class I topical corticosteroid compositions. *See* Exh. 2, Declaration of Dr. Gans, p. 3. Dr. Gans attests to the fact that altering the PE Ratio resulted in an unexpected rise from Class II to Class I, achieving super potency. *See* Exh. 2, Declaration of Dr. Gans, p. 4.

Even assuming *arguendo* that the Examiner has met the *prima facie* case of obviousness, Applicant refutes this with unexpected results (as discussed above). Prior to the FDA's approval of Vanos™ (the composition of the present invention) in February 2005, no fluocinonide product achieved super-high potency as a Class I corticosteroids. The FDA published the *Guidance for Industry* in 1995 setting forth the requirements for *in vivo* bioequivalence of topical dermatologic corticosteroids. *See* Exh. 2, Declaration of Dr. Gans, Exh. B. The guidelines set forth the use of vasoconstrictor assays to illustrate a composition's strength and equivalence to a reference drug. *Id.* The FDA has listed Vanos™ as a reference listed drug (RLD), against which all future abbreviated new drug applications (ANDA) for fluocinonide Class I drugs will be measured to show bioequivalence. *See* Exh. 3.

Therefore, based upon the fact that the cited reference fails to teach or suggest each and every claim element and the unexpected Class I designation of the composition of the present invention, the claims are not obvious over Poulsen. Applicant respectfully submits that this rejection has been overcome and should be removed.

PAGE 10/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

B. Claims 1, 2, 4-10, and 13-19 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Poulsen (US 3,934,013) in view of Bennett (J. of Pharmacy and Pharmacology, vol. 37, no. 3, 1985, pp. 298-304).

Applicant respectfully traverses this rejection. The Examiner fails to establish a *prima facie* case of obviousness based on Poulsen in view of Bennett with regard to the present invention.

As discussed above, Poulsen fails to teach or suggest two or more penetration enhancers, a PE Ratio of at least about 0.90 and above, and the novel and critical factors that are used in the PE ratio calculation or that the PE Ratio correlates with particular vasoconstrictor scores. Bennett does not make up for these deficiencies and also fails to teach or suggest the claimed invention on its own.

Bennett fails to teach or suggest the Result-Effective Variable, PE Ratio or a composition with a PE Ratio of at least about 0.90. For optimization of a particular Result-Effective Variable (such as the PE Ratio) to be considered obvious, the particular variable must first be recognized, which is not the case with the prior art of record. MPEP §2144.05. Additionally, Bennett fails to teach or suggest the specific components of the PE Ratio or that such a ratio correlates between improved potency and unexpectedly high vasoconstrictor scores. In fact, none of the taught compositions have the claimed PE Ratio of at least about 0.90. As discussed above and herewith submitted is a declaration by Dr. Gans showing that vasoconstrictor scores serve as a measure of the potency of a drug composition and that a PE Ratio of at least about 0.90 and above surprisingly resulted in an average vasoconstrictor score of 85, which is above the minimum

PAGE 11/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

score required by the FDA for Class I topical corticosteroid compositions. *See* Exh. 2, Declaration of Gans, p. 3. Further, Dr. Gans attests to the fact that altering the PE Ratio resulted in an unexpected rise from Class II to Class I and super potency. *See* Exh. 2, Declaration of Dr. Gans, p. 4.

Additionally, even assuming *arguendo* that the Examiner has met the *prima facie* case of obviousness, Applicant refutes this with unexpected results. The declaration by Dr. Gans shows that altering the PE Ratio of (penetration enhancers), to (penetration enhancers and solvent and emulsifiers), resulted in an unexpected rise from Class II to Class I. *See* Exh. 2, Declaration of Dr. Gans, p. 4.

Therefore, based upon the fact that the cited references fail to teach or suggest each and every claim element and the unexpected Class I designation of the composition of the present invention, the claims are not obvious over Poulsen in view of Bennett. Applicant respectfully submits that this rejection has been overcome and should be removed.

C. Claims 8-9 have been rejected under 35 U.S.C. §103(a) as being "unpatentable over Poulsen (US 3,934,013) as applied to claims 1-7 and 10, 13-19 above, and further in view of the PDR entries of Lidex-Synalar."

As discussed above, Poulsen fails to teach or suggest two or more penetration enhancers, a PE Ratio of 0.90 and above, and the novel and critical factors that are used in the PE Ratio calculation or that the PE Ratio correlates with particular vasoconstrictor scores.

PAGE 12/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

Further, the PDR reference when combined with Poulsen does not make up for the elements missing from Poulsen. Specifically, the PDR reference fails to teach the claimed PE Ratio of 0.90 and above. Moreover, the PDR reference cited by the Examiner is for Lidex®, which is a Class II steroid. *See* Table II, Specification, p. 11. In contrast, the present invention pertains to a composition having one or more corticosteroid, two or more penetration enhancers, and one or more solvents and emulsifiers with a PE Ratio of 0.90 and above, which yields a Class I (super-high range of potency) topical corticosteroid compositions. *See* Exh. 4, Label Approved by the FDA, p. 2. Table 2 of the specification shows the unexpected ability to produce vasoconstrictor scores for Class I drugs using the components of the present invention in the specified PE Ratio. Specification, p. 11, paragraph 27. Therefore, none of Poulsen, the PDR reference, or the combination of references teach or suggest all of the claim elements and there is no teaching or suggestion to combine the references.

The Examiner also asserts that "optimization of amounts of the penetration enhancers [sic] the optimization of a result effective parameter, e.g., amounts of the penetration enhancers, is considered within the skill of the artisan" citing *In re Boesch*, 205 USPQ 215 (CCPA 1980). The Examiner's argument is misplaced. Poulsen is silent as to two or more penetration enhancers, the PE Ratio, and a PE Ratio of at least about 0.90, and the PDR is silent as to the PE Ratio and a PE Ratio of at least about 0.90. No Result-Effective Variable has been recognized in the prior art and thus, no determination of the optimum or workable ranges of the variable may be characterized as routine experimentation or be considered within the skill of the artisan. MPEP §2144.05. Therefore, the prior art of record fails to render the claims obvious.

Additionally, as discussed above, even assuming *arguendo* that the Examiner has met the *prima facie* case of obviousness, Applicant refutes this with unexpected results. The declaration

PAGE 13/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

by Dr. Gans shows that altering the PE Ratio resulted in an unexpected rise from Class II to Class I. *See* Exh. 2, Declaration of Dr. Gans, p. 4.

Therefore, based upon the fact that the cited references fail to teach or suggest each and every claim element and the unexpected Class I designation of the composition of the present invention, the claims are not obvious over Poulsen or in further view of the PDR entries of Lidex-Synalar. Applicant respectfully submits that this rejection has been overcome and should be removed.

PAGE 14/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02

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CONCLUSION

In view of the foregoing remarks, Applicant respectfully requests consideration and allowance of the pending claims. Finally, Applicant respectfully submits a request for a personal interview with the Examiner, in order to further resolve any outstanding issues.

Authorization of Deposit Account

The Commissioner is hereby authorized to charge any fees which may be required during the entire pendency of this application, or credit any overpayment, to Deposit Account No. 18-0586. This authorization also hereby includes a request for any extensions of time of the appropriate length required upon the filing of any reply during the entire pendency of this application.

I hereby certify that this paper and the papers referred to herein as being transmitted, submitted, or enclosed herewith in connection with U.S. Serial No. 10/825,977 is/are being facsimile transmitted to the United States Patent and Trademark Office fax number 571-273-8300 on the date shown below.

Tamara Yorita

Date of Facsimile Transmission: November 16, 2007.

Respectfully submitted,
REED SMITH LLP

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PAGE 15/90 * RCVD AT 11/16/2007 4:19:05 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/4 * DNIS:2738300 * CSID:2158511420 * DURATION (mm-ss):14-02